

amendments can be found on page 37, lines 3-6. In addition, Claims 59 and 60 have been amended to incorporate the structure of Formula (IB) and the definitions for the substituents therein. Support for this amendment can be found on page 27, line 1 through page 29, line 23. Therefore, the rejection of claims 59 and 60 under 35 U.S.C. §112, second paragraph, is obviated and should be withdrawn.

The Examiner has rejected claim 58 under 35 U.S.C. §102(b) as being anticipated by Janiak (US Patent No. 3,810,988). Applicants respectfully traverse this rejection. Compounds 1, 3-9 and 16-56 of Janiak do not anticipate Claim 58 because Applicants' compound has a group of $\text{-NH-C(O)-NHC}_2\text{H}_5$ at the 2-position of the benzothiazole ring, whereas the compounds disclosed at columns 2 and 3 of Janiak and compounds 1, 3-9 and 16-56 of Janiak have different groups at the 2-position. Compounds 2 and 13 of Janiak do not anticipate Claim 58 because Applicants' compound does not include a $\text{-O-C}_2\text{H}_5$ group at the 6-position of the benzothiazole ring. Compound 10 of Janiak does not anticipate Claim 58 because in Applicants' compound, when W=OCH_3 , the OCH_3 substituent is located at the 6-position of the benzothiazole compound or when $\text{R}^2=\text{OCH}_3$ in Applicants' compound, the OCH_3 substituent is located at the 5-position of the benzothiazole ring, whereas in Janiak's compound 10 the OCH_3 is in the 7-position. Compound 11 of Janiak does not anticipate Claim 58 because in Applicants' compound, the possibilities for R^1 do not include chlorine. Claim 58 has been amended to proviso out compounds 12 and 15 of Janiak. Therefore, the rejection of claim 58 under 35 U.S.C. §102(b) over Janiak is obviated and should be withdrawn.

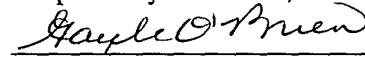
No fees are due for the instant amendment since the total number of claims after entry of the amendments hereinabove is not more than the total number of claims that Applicants have paid for to date.

Based upon the foregoing, Applicants believe that claims 58-60 are in condition for allowance. Prompt and favorable action is earnestly solicited.

If the Examiner believes that a telephone conference would advance the condition of the instant application for allowance, Applicants invite the Examiner to call Applicants' agent at the number noted below.

Date: January 17, 2003

Respectfully submitted,



Gayle B. O'Brien
Agent for Applicants
Reg. No. 48,812

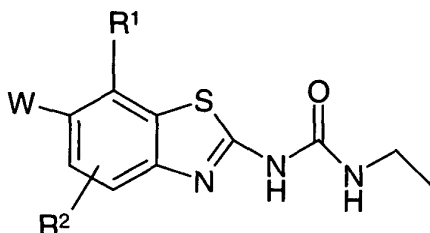
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APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

58. (Amended) A compound of the formula

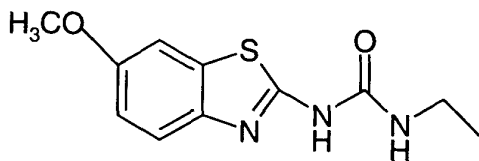
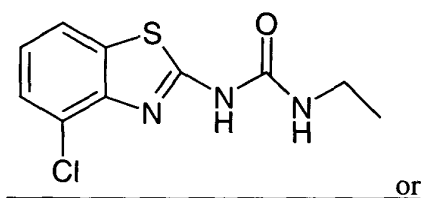


wherein W is H, -OCF₃, -O-Et, F, CH₃, -OCH₃, -SO₂-Me, NH₂, -NH-C(O)-Me, -NH-CH₂-phenyl, -NH-S(O)₂-2-thienyl, -NH-S(O)₂-(3,5-dimethylisoxazol-4-yl), -NH-S(O)₂-Me, -NH-S(O)₂-CH₂-phenyl, -NH-C(O)-O-CH₂-CCl₃, -NH-C(O)-O-CH₂-Ph, -NH-C(O)-O-Me or NO₂;

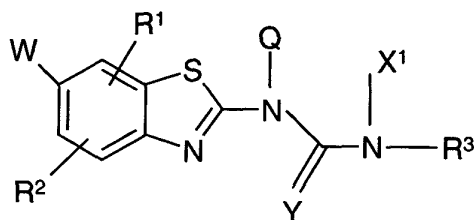
R¹ is H, F or -CH₂-S(O)₂-phenyl; and

R² is H, 4-Cl, 4-methyl, 5-methyl, 5-Cl, 5-F or 5-OCH₃[.]

provided that the compound is not



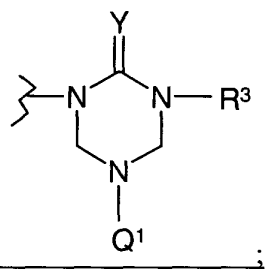
59. (Amended) A method of using a compound of formula (IB)



(IB)

or a pharmaceutically acceptable salt thereof, wherein,

Q is H or represents a bond which is taken together with X¹ and the two nitrogen atoms to which Q and X¹ are attached and the C=Y group to which the two nitrogen atoms are attached to form

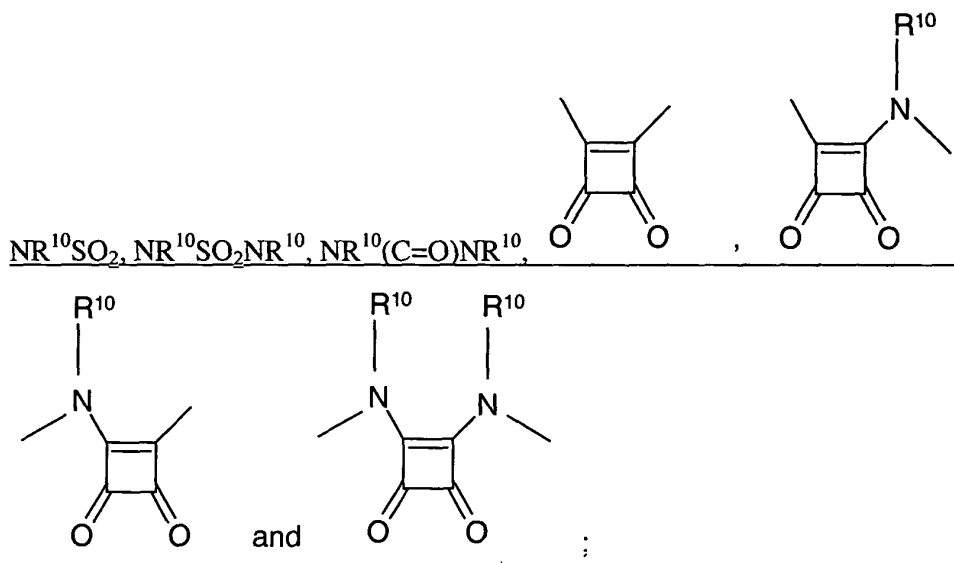


Q¹ is (C₁-C₆) alkyl;

Y is O or S;

W is H, Cl, Br, I, NO₂, CN, SCN, OCF₃, -X_q-(C(R¹⁰)₂)_a-Y¹_q-(C(R¹⁰)₂)_a-Z¹_q, or an optionally substituted group selected from the group consisting of alkyl, alkenyl, alkynyl, heterocycl-alkenyl, and heterocycl-alkynyl;

Y¹ and X are each independently selected from the group consisting of phenyl, heterocycl, NR¹⁰, O, S, SO, SO₂, CF₂, CFR, C=O, (C=O)NR¹⁰, SONR¹⁰, SO₂NR¹⁰(C=O), NR¹⁰SO,



q for each occurrence is independently 0 or 1;

a for each occurrence is independently 0 or an integer from 1 to 5;

R^{10} for each occurrence is independently selected from the group consisting of H, optionally substituted aryl, optionally substituted heterocyclyl and an optionally substituted alkyl group optionally substituted with one or more of the following: a C_{1-6} alkyl group optionally substituted by one or more hydroxy, halo or optionally substituted amino; a C_{1-6} alkoxy group optionally substituted by one or more hydroxy, halo or optionally substituted amino; hydroxy; halo; or optionally substituted amino;

Z^1 is H, optionally substituted alkyl, optionally substituted aryl or optionally substituted heterocyclyl;

X^1 is hydrogen, alkyl, hydroxyalkyl or represents a bond which is taken together with R^3 as described below or represents a bond which is taken together with Q as described above;

R^1 and R^2 are each independently hydrogen, halogen, hydroxy, nitro, cyano, COOH , COOX^3 , SX^3 , SO_2X^3 , SOX^3 , $\text{C}(\text{O})\text{X}^3$, $\text{NHC}(\text{O})\text{X}^3$, $\text{C}(\text{O})\text{NHX}^3$, NHSO_2X^3 or selected from an optionally substituted group consisting of alkyl, alkenyl, alkynyl, alkoxy, amino, NHX^3 , NX^3X^3 , alkylamino, arylamino, heterocyclylamino, alkylthio, alkylsulfonato, aryl, aryloxy, arylalkyl, arylalkenyl, arylalkynyl, arylalkyloxy, heterocyclyl, heterocycliloxy, heterocyclyl-alkyl, heterocyclyl-alkenyl, heterocyclyl-alkynyl, heterocyclyl-alkoxy, heterocyclylthio,

heterocyclisulfinyl, heterocyclisulfonyl, cycloalkyl, $-(CH_2)_m-(CHX^2)CN$, $-(CH_2)_m-(CHX^2)COOH$, $-(CH_2)_m-(CHX^2)COOX^3$, $-(CH_2)_m-(CHX^2)SO_2X^3$, $-(CH_2)_m-(CHX^2)C(O)X^3$, $-(CH_2)_m-(CHX^2)C(O)NHX^3$ and $-(CH_2)_m-(CHX^2)NHSO_2X^3$;

where m is 0 to 4;

X^2 for each occurrence is independently H or an optionally substituted moiety selected from the group consisting of alkyl, alkenyl, alkynyl, carbonyl, $S(O)_p$ alkyl, $S(O)_p$ aryl, $S(O)_p$ heterocyclyl, amino, alkoxy, alkylthio, arylthio, perhaloalkyl, aryl, aryloxy, arylalkyl, arylalkyloxy, heterocyclyl and heterocyclyl-alkyl;

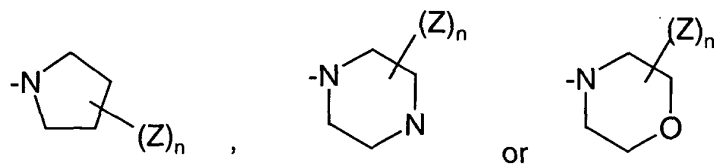
p is 0, 1 or 2;

X^3 for each occurrence is independently H or an optionally substituted moiety selected from the group consisting of mono- or di-alkylamino, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl and heterocyclyl-alkyl;

or when R^1 is in the 7-position of the benzothiazole ring, R^1 and W can be taken together with the carbon atoms to which they are attached to form an optionally substituted 5- or 6-membered heterocyclyl ring;

R^3 is hydrogen, or an optionally substituted moiety selected from the group consisting of carbonyl, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heterocyclyl-alkyl, heterocyclyl-heterocyclyl, heterocyclyl-cycloalkyl, amino, alkylamino, arylamino, alkoxy, thioalkoxy and acyl;

or R^3 and X^1 are taken together with the nitrogen atom to which they are attached to form



where Z for each occurrence is independently selected from the group consisting of oxo, or an optionally substituted moiety selected from the group consisting of $-C(O)(C_1-C_6)alkyl$, $-C(O)aryl$, $-C(O)N(C_1-C_6)alkyl$, $-C(O)N-aryl$, $(C_1-C_6)alkyl$, $(C_2-C_6)alkenyl$, $(C_2-C_6)alkynyl$, amino, mono- or di- $(C_1-C_6)alkylamino$, $-COO(C_1-C_6)alkyl$, pyridyl, phenyl, phenyl $(C_1-C_6)alkyl$ and phenyl $(C_1-C_6)alkenyl$;

where each of the optionally substituted moieties described hereinabove is optionally substituted by one or more substituents each independently selected from the group

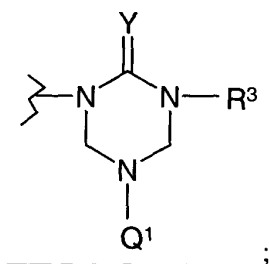
consisting of oxo, amino, nitro, mono- or bi-(C₁-C₆)alkylamino, hydroxy, nitrile, chloro, fluoro, bromo, iodo, CF₃, (C₁-C₆)alkyl, -C(O)(C₁-C₆)alkyl, -COOH, -COO(C₁-C₆)alkyl, -S-(C₁-C₆)alkyl, -S-aryl, (C₁-C₆)alkoxy, -SO₂NH₂, phenyl, phenyl(C₁-C₆)alkyl, -O-(C₁-C₆)alkyl-OH, -O-(C₁-C₆)alkyl-O-(C₁-C₆)alkyl, -O-(C₂-C₆)alkyl-N-((C₁-C₆)alkyl)_n, -N-(C₁-C₆)alkyl-OH, -N-(C₁-C₆)alkyl-O-(C₁-C₆)alkyl, -C(O)NH₂, -C(O)N((C₁-C₆)alkyl)_n, -S(O)_n(C₁-C₆)alkyl, -S(O)_nO_naryl, -S(O)_nheterocyclyl, and heterocyclyl, where the alkyl groups mentioned herein optionally have one or more unsaturated bonds in the alkyl portion;

n is 0, 1 or 2;

as a replacement therapy for anti-inflammatory glucocorticosteroid therapy in a patient undergoing anti-inflammatory glucocorticosteroid therapy comprising the steps of replacing a glucocorticosteroid with a compound of formula (IB) or a pharmaceutically acceptable salt thereof[.] and systemically administering the compound of formula (IB) or a pharmaceutically acceptable salt thereof.

60. (Amended) A method of using a compound of formula (IB) or a pharmaceutically acceptable salt thereof, wherein,

Q is H or represents a bond which is taken together with X¹ and the two nitrogen atoms to which Q and X¹ are attached and the C=Y group to which the two nitrogen atoms are attached to form

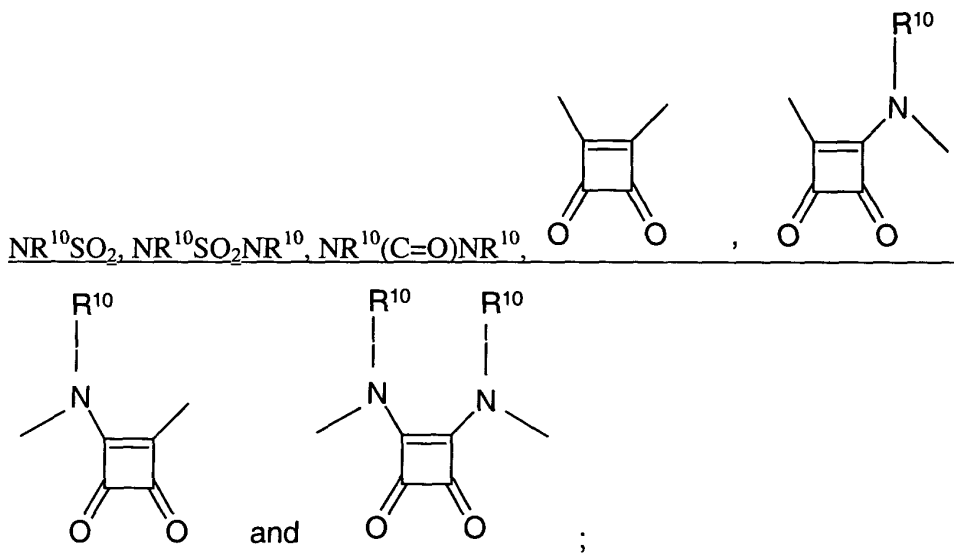


Q¹ is (C₁-C₆) alkyl;

Y is O or S;

W is H, Cl, Br, I, NO₂, CN, SCN, OCF₃, -X_q-(C(R¹⁰)₂)_a-Y¹_q-(C(R¹⁰)₂)_a-Z¹_q, or an optionally substituted group selected from the group consisting of alkyl, alkenyl, alkynyl, heterocyclyl-alkenyl, and heterocyclyl-alkynyl;

Y^1 and X are each independently selected from the group consisting of phenyl, heterocyclyl, NR^{10} , O, S, SO, SO_2 , CF_2 , CFR, C=O, $(C=O)NR^{10}$, $SONR^{10}$, $SO_2NR^{10}(C=O)$, $NR^{10}SO$,



q for each occurrence is independently 0 or 1;

a for each occurrence is independently 0 or an integer from 1 to 5;

R^{10} for each occurrence is independently selected from the group consisting of H, optionally substituted aryl, optionally substituted heterocyclyl and an optionally substituted alkyl group optionally substituted with one or more of the following: a C_{1-6} alkyl group optionally substituted by one or more hydroxy, halo or optionally substituted amino; a C_{1-6} alkoxy group optionally substituted by one or more hydroxy, halo or optionally substituted amino; hydroxy; halo; or optionally substituted amino;

Z^1 is H, optionally substituted alkyl, optionally substituted aryl or optionally substituted heterocyclyl;

X^1 is hydrogen, alkyl, hydroxyalkyl or represents a bond which is taken together with R^3 as described below or represents a bond which is taken together with Q as described above;

R^1 and R^2 are each independently hydrogen, halogen, hydroxy, nitro, cyano, $COOH$, $COOX^3$, SX^3 , SO_2X^3 , SOX^3 , $C(O)X^3$, $NHC(O)X^3$, $C(O)NHX^3$, $NHSO_2X^3$ or selected from an optionally substituted group consisting of alkyl, alkenyl, alkynyl, alkoxy, amino, NHX^3 , NX^3X^3 ,

alkylamino, arylamino, heterocyclylamino, alkylthio, alkylsulfonato, aryl, aryloxy, arylalkyl, arylalkenyl, arylalkynyl, arylalkyloxy, heterocyclyl, heterocyclyoxy, heterocyclyl-alkyl, heterocyclyl-alkenyl, heterocyclyl-alkynyl, heterocyclyl-alkoxy, heterocyclylthio, heterocyclylsulfinyl, heterocyclylsulfonyl, cycloalkyl, $-(CH_2)_m-(CHX^2)CN$, $-(CH_2)_m-(CHX^2)COOH$, $-(CH_2)_m-(CHX^2)COOX^3$, $-(CH_2)_m-(CHX^2)SO_2X^3$, $-(CH_2)_m-(CHX^2)C(O)X^3$, $-(CH_2)_m-(CHX^2)C(O)NHX^3$ and $-(CH_2)_m-(CHX^2)NHSO_2X^3$;

where m is 0 to 4;

X^2 for each occurrence is independently H or an optionally substituted moiety selected from the group consisting of alkyl, alkenyl, alkynyl, carbonyl, $S(O)_p$ alkyl, $S(O)_p$ aryl, $S(O)_p$ heterocyclyl, amino, alkoxy, alkylthio, arylthio, perhaloalkyl, aryl, aryloxy, arylalkyl, arylalkyloxy, heterocyclyl and heterocyclyl-alkyl;

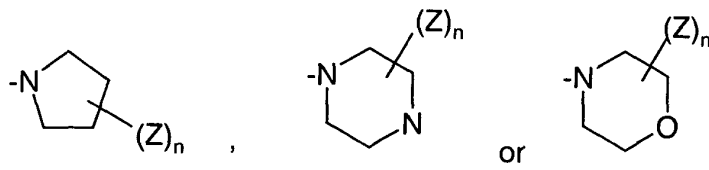
p is 0, 1 or 2;

X^3 for each occurrence is independently H or an optionally substituted moiety selected from the group consisting of mono- or di-alkylamino, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl and heterocyclyl-alkyl;

or when R^1 is in the 7-position of the benzothiazole ring, R^1 and W can be taken together with the carbon atoms to which they are attached to form an optionally substituted 5- or 6-membered heterocyclyl ring;

R^3 is hydrogen, or an optionally substituted moiety selected from the group consisting of carbonyl, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heterocyclyl-alkyl, heterocyclyl-heterocyclyl, heterocyclyl-cycloalkyl, amino, alkylamino, arylamino, alkoxy, thioalkoxy and acyl;

or R^3 and X^1 are taken together with the nitrogen atom to which they are attached to form



where Z for each occurrence is independently selected from the group consisting of oxo, or an optionally substituted moiety selected from the group consisting of $-C(O)(C_1-C_6)alkyl$, $-C(O)aryl$, $-C(O)N(C_1-C_6)alkyl$, $-C(O)N-aryl$, $(C_1-C_6)alkyl$, $(C_2-C_6)alkenyl$, $(C_2-C_6)alkynyl$, amino, mono- or di- $(C_1-C_6)alkylamino$,

-COO(C₁-C₆)alkyl, pyridyl, phenyl, phenyl(C₁-C₆)alkyl and phenyl(C₁-C₆)alkenyl;
where each of the optionally substituted moieties described hereinabove is optionally
substituted by one or more substituents each independently selected from the group
consisting of oxo, amino, nitro, mono- or bi-(C₁-C₆)alkylamino, hydroxy, nitrile, chloro,
fluoro, bromo, iodo, CF₃, (C₁-C₆)alkyl, -C(O)(C₁-C₆)alkyl, -COOH, -COO(C₁-C₆)alkyl,
-S-(C₁-C₆)alkyl, -S-aryl, (C₁-C₆)alkoxy, -SO₂NH₂, phenyl, phenyl(C₁-C₆)alkyl, -O-(C₁-
C₆)alkyl-OH, -O-(C₁-C₆)alkyl-O-(C₁-C₆)alkyl, -O-(C₂-C₆)alkyl-N-((C₁-C₆)alkyl)_n,
-N-(C₁-C₆)alkyl-OH, -N-(C₁-C₆)alkyl-O-(C₁-C₆)alkyl, -C(O)NH₂, -C(O)N((C₁-
C₆)alkyl)_n, -S(O)_n(C₁-C₆)alkyl, -S(O)O_naryl, -S(O)_nheterocyclyl, and heterocyclyl, where
the alkyl groups mentioned herein optionally have one or more unsaturated bonds in the
alkyl portion;

n is 0, 1 or 2;

in conjunction with glucocorticosteroid therapy in a patient undergoing glucocorticosteroid therapy comprising the step of replacing a portion of the amount of glucocorticosteroid administered to said patient[.] and systemically administering the glucocorticosteroid and compound of formula (IB) or a pharmaceutically acceptable salt thereof.